Remarks

Status of the Claims

Claims 1, 2, 7-18 are pending. Claims 1 and 2 are rejected under Section 112, first paragraph. Claims 1-2 and 7-18 have been amended. Claims 7-18 are allowed. Applicants have added new claims 19-24.

Rejoinder of Group II

The Examiner had restricted the invention into the two groups, in response to which Applicants had elected Group I and canceled claims 4-6 from Group II (drawn to various methods of treating diseases, classified in class 514 and various subclasses).

As was previously requested in the Applicants' November 7, 2006 Response to Office Action, Applicants respectfully re-request rejoinder of claims 4-6 with the elected group because the pending claims are now allowable.

Rejection under Section 112, First Paragraph

Claim 1 was rejected under 35 U.S.C. Section 112, first paragraph as being unpatentable. The Examiner has brought this rejection due to the use of the term "polymorph" in said claim.

Without stipulating to the substance of the rejection and solely to advance the prosecution of this application, Applicants have amended claim 1 to advance the prosecution of this application.

Claim 2 was rejected under 35 U.S.C. Section 112, first paragraph as being unpatentable. The Examiner has brought this rejection due to the use of the terms "pharmaceutical" composition with an "effective amount" in said claim. The Examiner stated that applicants' own 2003 article titled "Potent Non-Peptide Thrombin Receptor Antagonists" states that the "practicality of effectively blocking

thrombin receptor activation by the tethered ligand has been debated . . . . . the final answer will come only in efficacy models in the in vivo settings." (Chackalamannil et al., page 43).

In response, Applicants respectfully traverse this rejection. Applicants respectfully reiterate the FULL quotation cited by the Examiner as the following: "*Although* the final answer to this question will come only in efficacy models in the in vivo settings, *the following information suggests that this is an achievable goal.*" (Chackalamannil et al., page 43, column 1). The article recites the following on page 43, column 1 of the Chackalamannil et al.:

> High affinity peptide and non-peptide PAR-1 antagonists have been reported. Several of these inhibit thrombin and peptide agonist-induced platelet aggregation. The potential antirestenosis utility for a thrombin receptor antagonist has been established in a proof-of-principle rat restenosis model (see Zhang et al. J. Med. Chem. 2001, 44, 1021), and studies performed in baboons with a thrombin receptor antibody indicates that arterial thrombosis can be inhibited by inactivation of PAR-1 without affecting template bleeding time. (see Cook et al. Circulation 1995, 91, 2691).

Contrary to the Examiner's assertion pharmaceutical compositions in effective amounts are not enabled, Applicants respectively point to the cited passage above as proof that claim 2 is enabled as a pharmaceutical composition to effectively treat a disease or disorder. The above-cited passage points out two different instances where thrombin receptor antagonists have shown use against restenosis and arterial thrombosis. Furthermore, Applicants quote MPEP 2164.01 where it states that

> As long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. 112 is satisfied. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

Applicants respectively point the Examiner to page 69 of the specification, last paragraph, where it states that

> representative compounds of formula I were found to have thrombin receptor IC_{50} values (*i.e.*, the concentration at which a 50% inhibition of thrombin receptor was observed) of 1 to 1000 nM, preferably 1-100 nM, more preferably 1-20 nM. CB_2 Ki values range from 1 to 1000 nM, preferably 1-200 nM, more preferably 1-100 nM. For example, IC_{50} values of Example Nos. 8BU, 8CA, 8CB, 8CL, 17H, 20E, 20F, 20G and 20H range from 1-100 nM.

Rather than the 1996, Bernatowicz article to demonstrate the state of the art, Applicants respectfully suggest that the state of the art in pharmaceutical compositions of thrombin receptor antagonists is demonstrated in the Applicants' specification and claimed invention. Applicants point to pages 64-65 of the specification wherein pharmaceutical compositions of the compounds of Formula I, whether alone or in combination with other agents (*e.g.*, aspirin and clopidogrel bisulfate), are described. In particular, on page 65, Example A provides a pharmaceutical composition and method of manufacture of said pharmaceutical composition as a tablet. Example B on page 65 provides a pharmaceutical composition and method of manufacture of said pharmaceutical composition as a capsule. Applicants point out that the excipients of both Examples A and B are well known to one of ordinary skill in the art as excipients used in pharmaceutical compositions. As required by MPEP 2164.01, applicants have provided in their specification at least one method of making and using the claimed pharmaceutical compositions of claim 2, thus mooting this rejection.

Therefore, applicants respectfully request the withdrawal of this Section 112, first paragraph rejection.

Conclusion

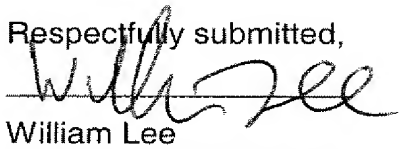
Applicants have overcome all the rejections of the outstanding Office Action. Hence, claims 1, 2 and 7-24 are in condition for allowance, which timely allowance the Examiner is respectfully requested.

Authorization

As this Amendment is being filed within the three-month period following the shortened statutory period for reply to the Office Action, the Commissioner is hereby petitioned for a three-month extension of time. The Commissioner is hereby authorized to draw the required amount from Applicants' deposit account no. 19-0365. Should any further extension or any other fee become necessary to render this Amendment timely filed and to allow entry of the Amendment, the Commissioner is hereby petitioned for such extension and is authorized to draw the required amount from Applicants' deposit account no. 19-0365.

Should the Examiner feel that a telephone conference with Applicants' representatives would assist the Examiner, she is invited to telephone the undersigned at anytime. Applicants request favorable consideration of the application and early allowance of the pending claims.

Respectfully submitted,



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